



Fatty Acid Oxidation (β oxidation regulaion & ω oxidation)

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INTENDED LEARNING OBJECTIVES (ILO)



By the end of this lecture the student will be able to:

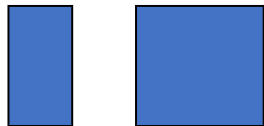
- 1. Illustrate the steps of odd number F.A oxidation**
- 2. Correlate defects in **propionate metabolism** to clinical disorders**
- 3. Discuss regulatory steps of FA oxidation**
- 4. Interpret the role of peroxisomes in oxidation of VLCFA and its clinical correlation.**
- 5. Discuss other types of FA oxidation and their clinical**

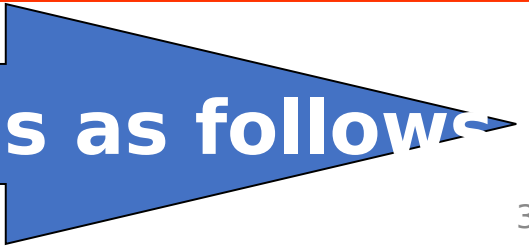


Odd number FA oxidation

Oxidation of FAs with an **odd number of
carbons:**

**The β -oxidation of a saturated odd FA proceeds
the same as even until the **final three carbons**
propionyl CoA is reached, it is metabolized by
a **three-step pathway****



three-step pathway proceeds as follows 



Steps:

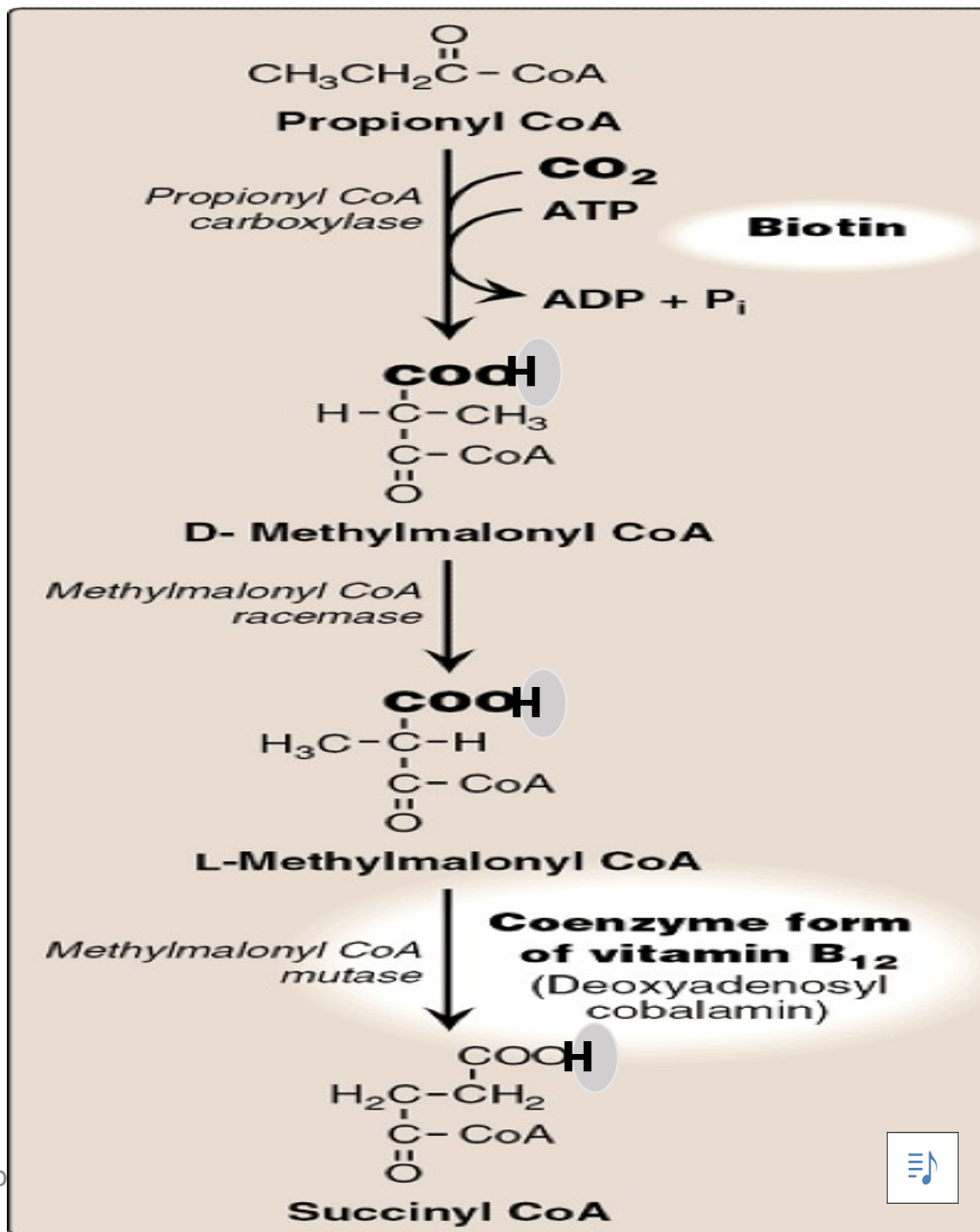
1-Synthesis of D-methylmalonyl CoA from propionyl CoA

2-Formation of L-methylmalonyl CoA

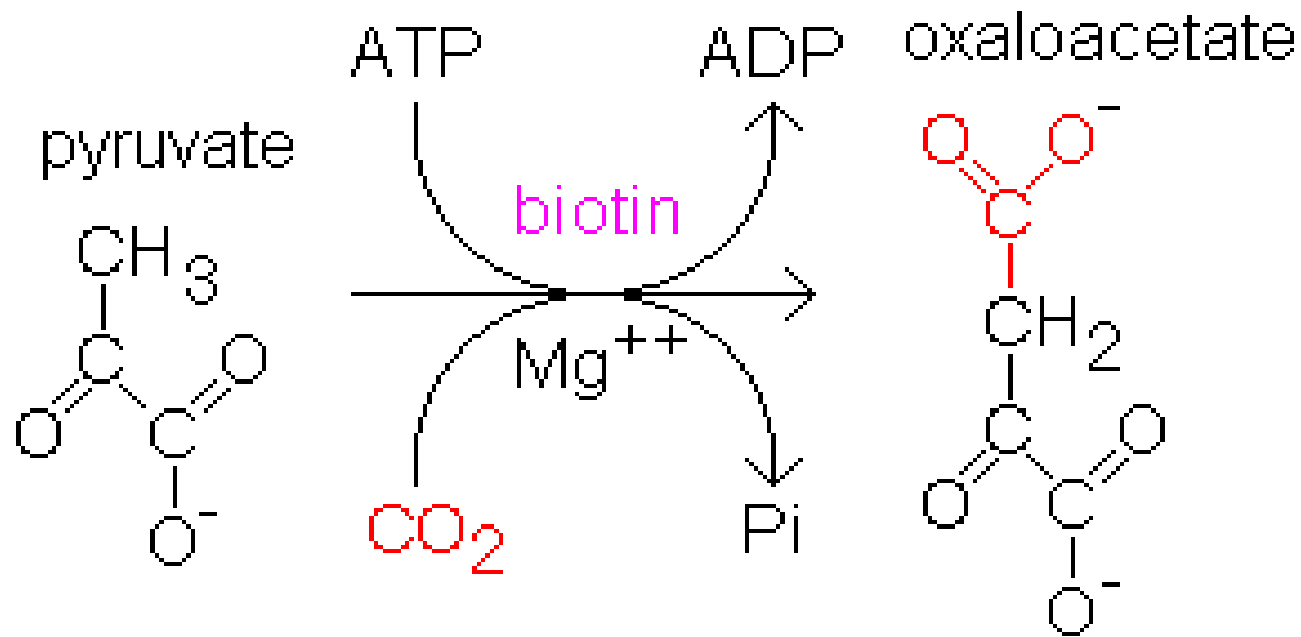
3- Synthesis of succinyl CoA. the Cs of L-MM CoA are rearranged, forming succinyl CoA, which enters (TCA) cycle.

[Note: This is the only example
of a gluconeogenic precursor

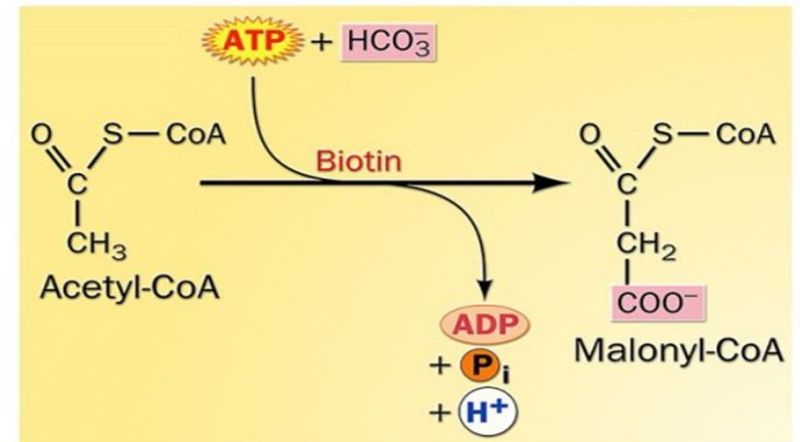
Cardio-pulmonary Mo



- Biotin is required for carboxylation reactions (CO_2 fixation reaction)
- Biotin is required for the enzymes
- Pyruvate carboxylase
- Acetyl CoA carboxylase
- Propionyl carboxylase



Reaction catalyzed by Acetyl CoA Carboxylase



Activation of acetate : Acetyl-CoA to malonyl CoA

Inborn errors of propionate metabolism

***Propionyl CoA
carboxylase
deficiency***

**Characterized by
propionic acidemia,
ketosis, lethargy,
vomiting, and ataxia**

**Methylmalonyl acidemia &
aciduria in early infancy**

**Characterized by accumulation of
methyl malonic acid in the body with
metabolic acidosis, vomiting, dyspnea,
dehydration and neurological
manifestations (mental retardation,
hypotonia, seizures, encephalopathy,
coma & death)**

**Due to deficiency of
vitamin B12**

**Due to defect in the
enzyme methylmalonyl
CoA mutase or
racemase**

Key question



A 8 month boy infant presents by his mother to emergency with vomiting, difficulty of breathing & convulsions. Examination revealed dyspnea, dehydration, mental retardation, hypotonia, and seizures. Laboratory investigation shows metabolic acidosis.

Which one of the following is suspected to be increased in his blood?

A. Glucose

☒ B. Cholesterol

C. Methylmalonyl CoA

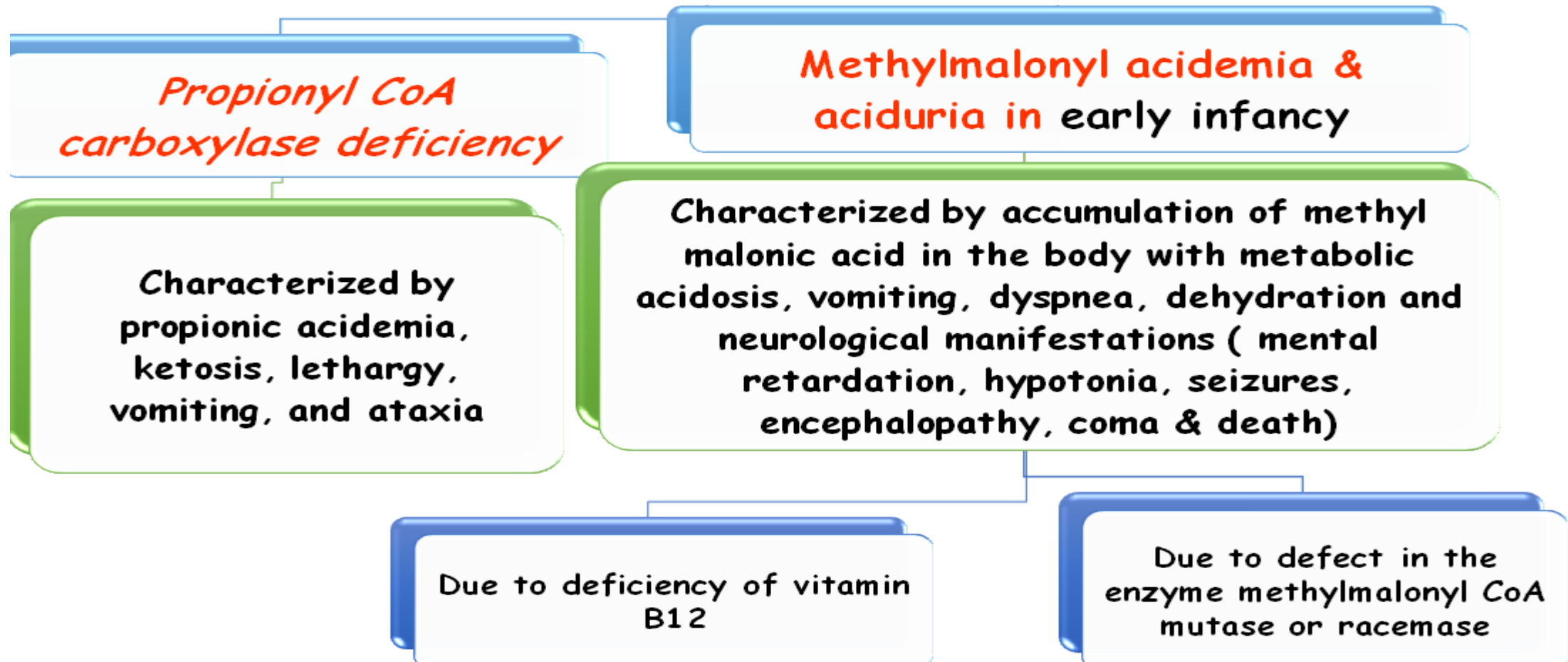
D. Succinyl CoA

E. Palmitic acid

Key question

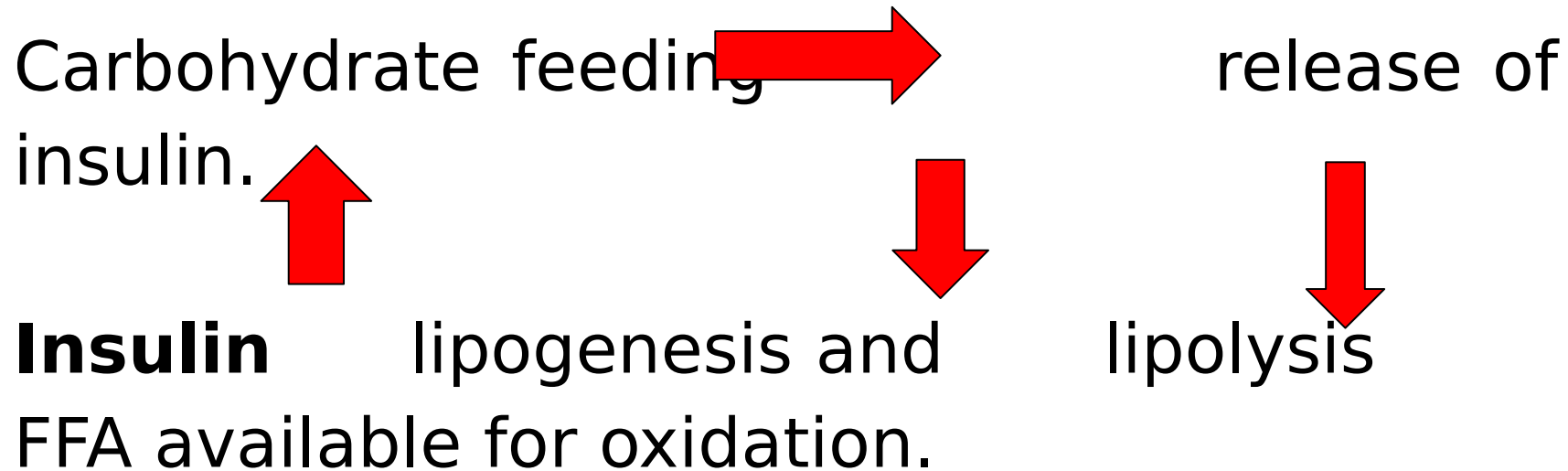


Explain on a biochemical basis Inborn errors of propionate metabolism



β oxidation regulation

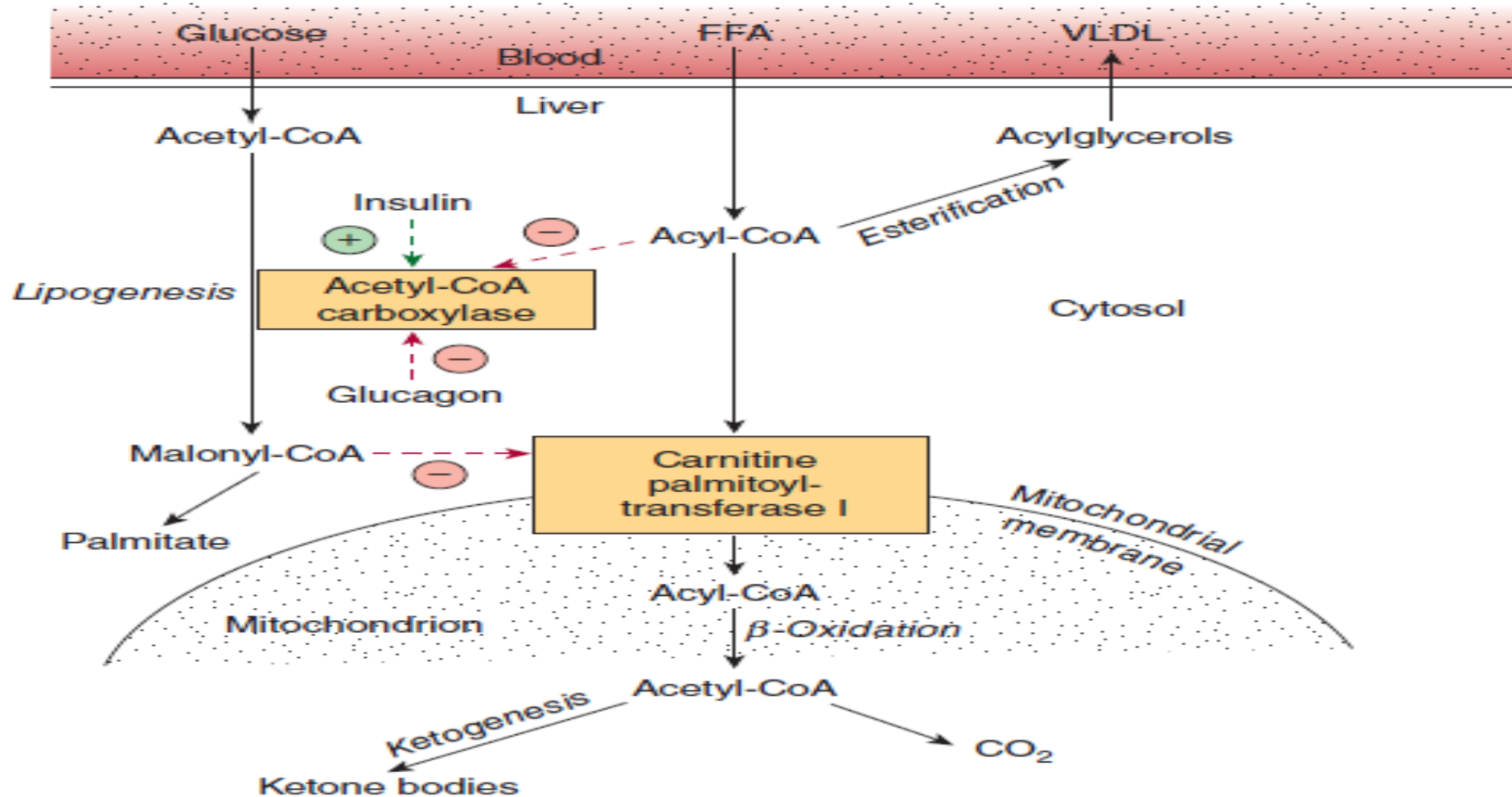
Hormonal regulation



Anti-insulin hormones produce the reverse thus increasing FFA available for oxidation.



β oxidation regulation



Malonyl CoA act as inhibitor of Carnitine Palmitoyl-Transferase I (CPTI) so inhibit β -fatty acid oxidation

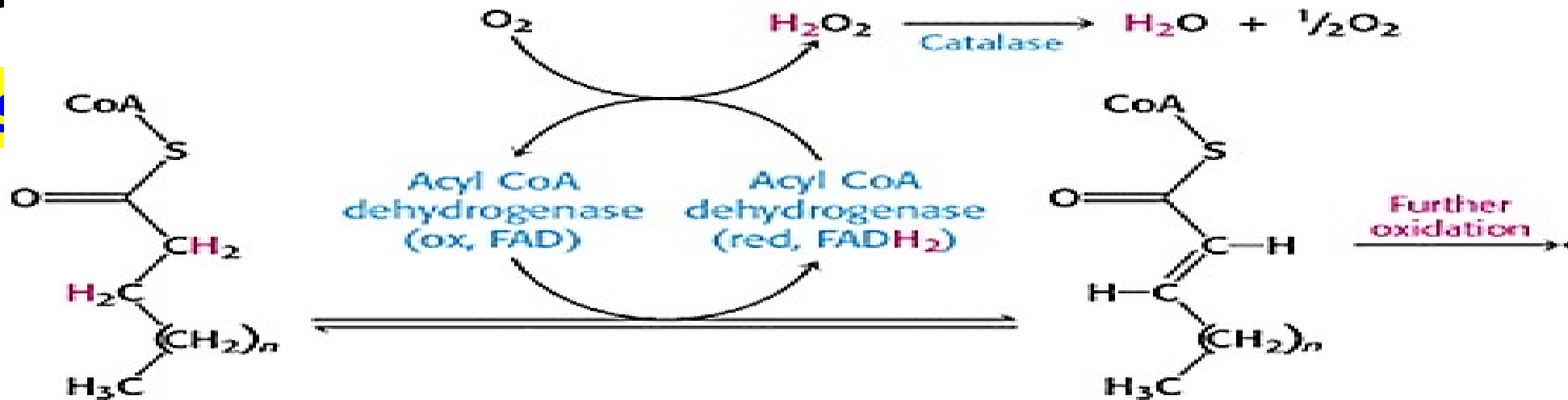


β oxidation in peroxisome

- It is a preliminary step shortening **the VLCFA $\geq 22C$,**

* **Shortened FA** is transferred to mitochondria for further oxidation **require FAD-containing acyl CoA**

oxidation



β oxidation in peroxisome



***In contrast to mitochondrial β -oxidation:**

Initial dehydrogenation in peroxisomes is **FAD-containing *acyl CoA oxidase*; where **FADH₂** produced is **oxidized by molecular oxygen** which is reduced to **H₂O₂** and **H₂O₂** is reduced to **H₂O** by ***catalase***. **No energy** is produced **at this step**.**



β oxidation in peroxisome



Zellweger syndrome

Genetic defects in the previous process leads to **accumulation of VLCFA in blood and tissues(brain, liver, and kidney) with production of neurological symptoms & face deformity.**

- **Death within 6 months**



Key question



Which one of the following is a genetic defects in the previous process leads to accumulation of VLCFA in blood and different tissues?



A. Refsum disease

B. Zellweger syndrome

C. Carnitine deficiency

D. Methylmalonyl CoA acidemia

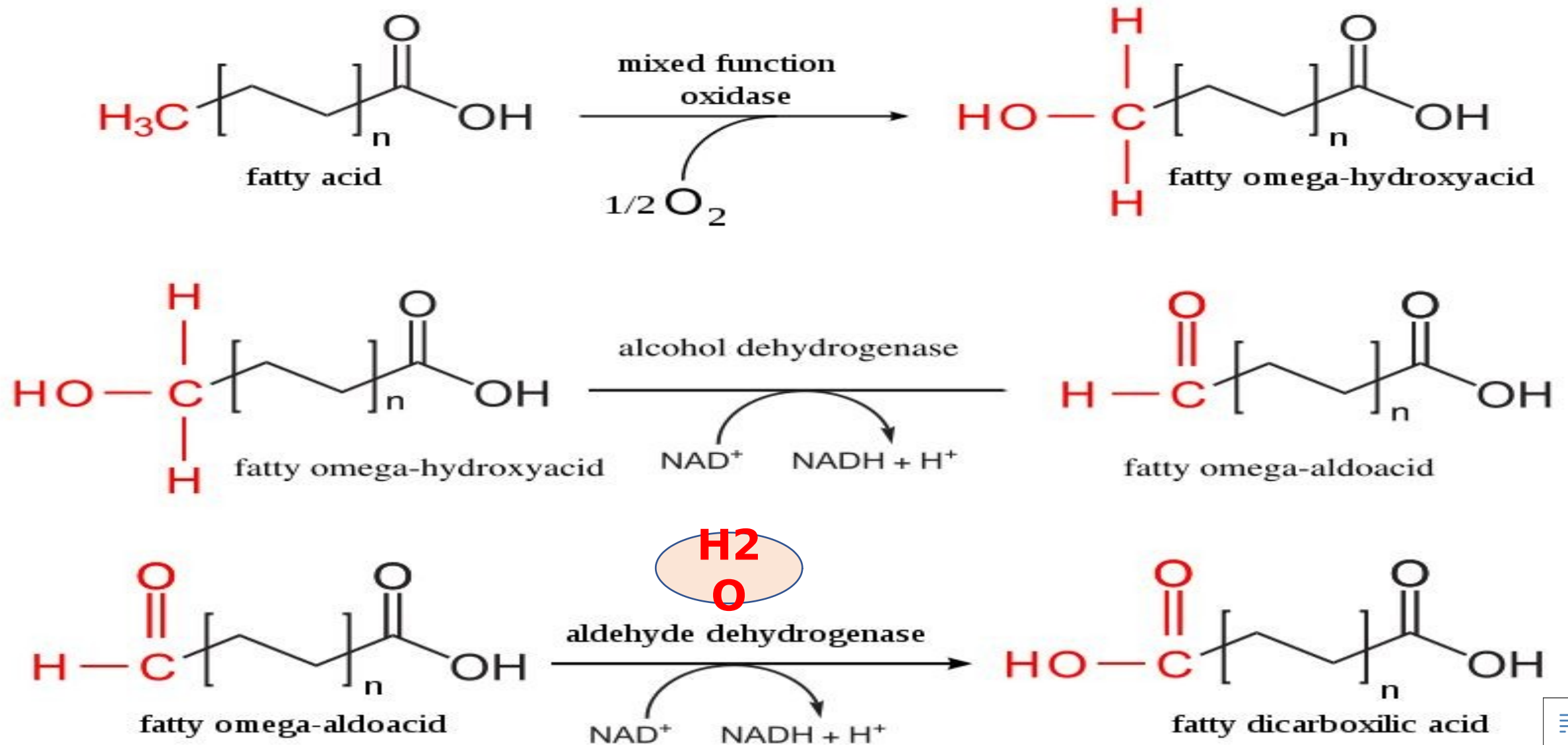
E. Propionyl CoA carboxylase deficiency

Omega (ω) oxidation

- It is a **minor** pathway of fatty acid oxidation.
- It occurs in smooth **ER** involving **cytochrome p450**
- Methyl terminus is oxidized to carboxyl group
- The Fatty acid converted into dicarboxylic F.A
- **Beta oxidation** proceed from both ends with

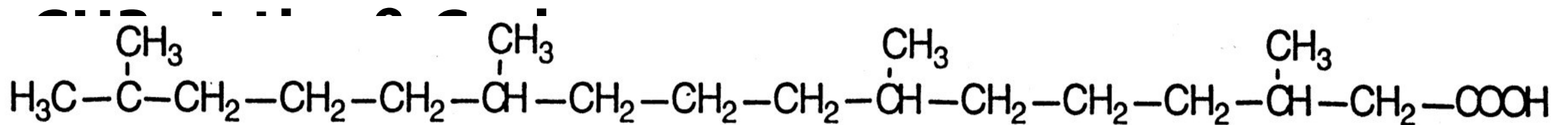


Steps of Omega (ω) oxidation



Alpha (α) oxidation

- It is a **minor** pathway.
- It is important only for oxidation of **methyated FA** (branched), e.g., **phytanic acid** (found in dairy products).
- β -Oxidation cannot occur due to the presence of

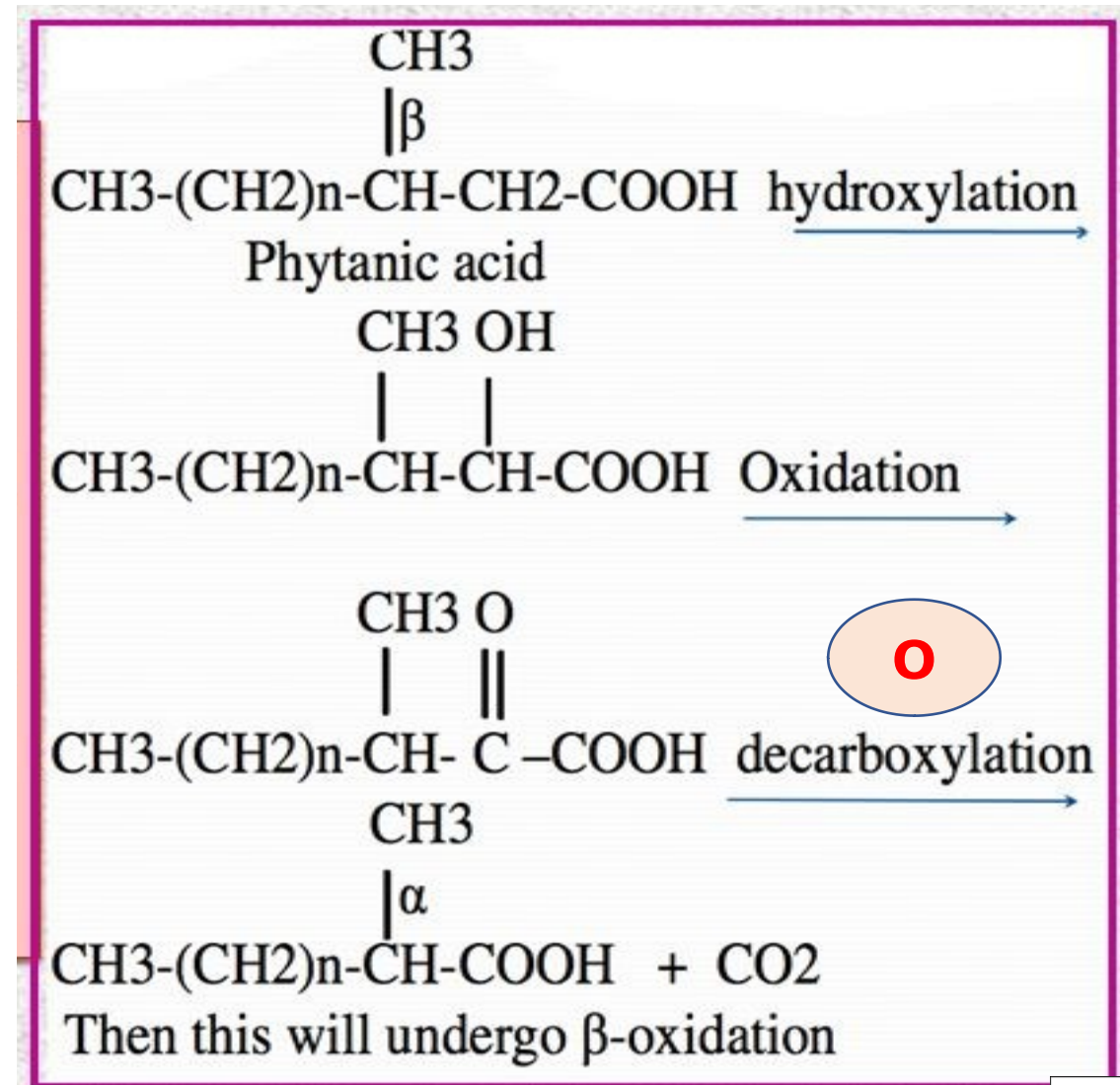


Phytanic acid



Alpha (α) oxidation

- The aim of the α -oxidation is to modify the shape of the FA in order to be able later to make β -oxidation.
- α -Oxidation **does not produce energy as it removes one carbon at a**

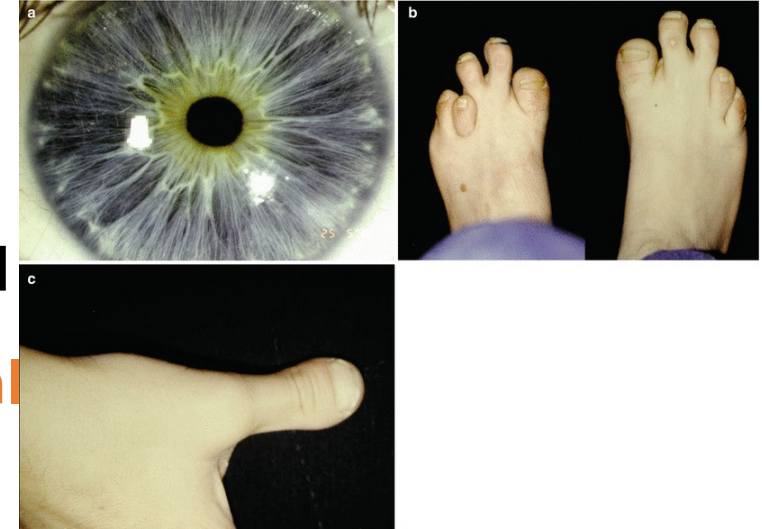


Alpha (α) oxidation



Refsum disease

Genetic defects in the previous process leads to **accumulation of phytanic acid** in the plasma and tissues. The symptoms are primarily **neurological like ataxia** with night blindness, deafness, dry scaly skin and shortened fingers or toes. Treatment involves dietary restriction to prevent disease progression.



Key question



Discuss on a biochemical basis Refsum disease

Refsum disease

Genetic defects in the previous process leads to **accumulation of phytanic acid** in the plasma and tissues. The symptoms are primarily **neurological like ataxia** with night blindness, deafness, dry scaly skin and shortened fingers or toes. **Treatment involves dietary restriction to prevent disease progression.**

Key points



1.Steps of odd number F.A oxidation

2.defects in propionate metabolism & clinical disorders

3. Regulatory steps of FA oxidation

4. The role of peroxisomes in oxidation of VLCFA and its clinical correlation.

5.other types of FA oxidation and their clinical

SUGGESTED TEXTBOOKS



- 1. "Lippincott's Illustrated Reviews in Biochemistry" by P.C.Champe, R.A.Harvey and D.R. Ferrier.**
- 2. "Harper's Biochemistry" by R.K.Murray, D.K.Granner, P.A. Mayes and V.W. Rodwell.**

Thank
you

